CLAIMS

What we claim is:

1. A cartridge for delivering a fluid sample to an analysis location comprising:

a housing having a closable sample entry port for receiving a fluid sample;

a holding chamber having a first end in communication with the entry port, the holding chamber having a second end with a capillary stop; wherein the analysis location is in communication with the capillary stop; and wherein the capillary stop selectively allows passage of the sample from the holding chamber to the analysis location;

an overflow chamber in communication with the holding chamber for handling overflow of incoming sample; and

a pump for providing a force to the fluid sample in the holding chamber, thereby allowing passage of the sample through the capillary stop.

2. The cartridge of claim 1 wherein the overflow chamber is located above the holding chamber and separated from the holding chamber by a holding chamber wall.

3. The cartridge of claim 1 wherein the communication between the overflow chamber and the holding chamber is through an orifice in the holding chamber wall.

4. The cartridge of claim 3 wherein the shape of the orifice is circular.

5. The cartridge of claim 3 wherein the orifice is circular with a diameter of about 100 microns to about 1000 microns.

6. The cartridge of claim 3 wherein the area of the orifice is larger than the area of the capillary stop.

7. The cartridge of claim 3 wherein the orifice has a lower resistance to fluid flow than does the capillary stop.

8. The cartridge of claim 3 wherein a roof of the holding chamber comprises a tape and the orifice comprises a hole in the tape.

9. The cartridge of claim 3 wherein the volume of the holding chamber between the orifice and the capillary stop corresponds substantially to the volume of the fluid sample.

10. The cartridge of claim 9 wherein the overflow chamber receives excess sample from the holding chamber through the orifice.

11. The cartridge of claim 1 further comprising a pre-sensor chamber between the capillary stop and the analysis location.

12. The cartridge of claim 11 wherein the cross-sectional area of the holding chamber is larger than the cross-sectional areas of the pre-sensor channel and the analysis location.

13. The cartridge of claim 11 further comprising a hydrophobic area between the analysis location and the pre-sensor chamber.

14. The cartridge of claim 13 wherein the hydrophobic area comprises a hydrophobic matrix coating selected from the group consisting of wax, petroleum gel, and non-polar organic film.

15. The cartridge of claim 13 wherein the hydrophobic area comprises a layer of material selected from the group consisting of polytetrafluoroethylene, plastic coated with polytetrafluoroethylene, polyimide treated with a fluoride ion-plasma, silicon dioxide coated with an organic compound, an alloy of tungsten and titanium, and silver coated with silver chloride.

16. The cartridge of claim 13 wherein the hydrophobic area comprises a layer of polytetrafluoroethylene.

17. The cartridge of claim 1 wherein the capillary stop has a rectangular shape. wherein the smallest dimension is about 100 microns to about 400 microns.

18. The cartridge of claim 1 wherein the overflow chamber has walls which are wetted when excess sample enters the overflow chamber.

19. The cartridge of claim 1 wherein excess sample is forced into the overflow chamber by closure of the entry port closure.

20. The cartridge of claim 1 wherein the wall surfaces of the holding chamber are corona treated.

21. The cartridge of claim 1 wherein the volume of the sample is in the range of 1 microliter to 1 milliliter.

22. The cartridge of claim 1 wherein the volume of the sample is in the range of 20 microliters to 50 microliters.

23. The cartridge of claim 1 wherein the volume of the overflow chamber is in the range of 0.2 microliters to 1 milliliter.

24. The cartridge of claim 1 wherein the volume of the overflow chamber is in the range of 1 microliter to 10 microliters.

25. The cartridge of claim 1 wherein the pump is in fluidic connection with the overflow chamber.

26. The cartridge of claim 1 wherein the force provided to the sample is a pneumatic force.

27. The cartridge of claim 1 which includes an upper housing, a lower housing, and a film coated on both sides with adhesive, the film interposed between the upper housing and the lower housing.

28. The cartridge of claim 1 wherein the holding chamber or the overflow chamber or both, or portions thereof, are treated to impart a high energy surface to the interior chamber surfaces.

29. The cartridge of claim 1 adapted for use with an analyzer.

30. The cartridge of claim 29 wherein the pump is actuated by an actuator element of the analyzer.

31. The cartridge of claim 1 further comprising a predetermined amount of reagent in the analysis location for mixing with the fluid sample.

32. The cartridge of claim 1 further comprising a circumferential well around the entry port for receiving spilled fluid sample.

33. The cartridge of claim 1 wherein the interior surfaces of the holding chamber and or the overflow chamber are corona treated.

34. The cartridge of claim 1 wherein the holding chamber has a lower interior surface to volume ratio than does the overflow chamber.

35. The cartridge of claim 1 wherein the entry port closure makes an air-tight seal when closed.

36. The cartridge of claim 1 further comprising a predetermined amount of reagent in the holding chamber for mixing with the sample.

37. The cartridge of claim 1 further comprising at least one sensor.

38. The cartridge of claim 1 in which the analysis location comprises at least one sensor.

39. A cartridge for delivering a fluid sample to an analysis location, comprising:

a housing containing a fluid path and having first and second sides, wherein at least one side contains at least one fluid channel, said first and second sides attached with a wall located therebetween, said wall and said channels providing the fluid path; and

a hydrophobic area comprising a portion of the fluid path, the hydrophobic area inhibiting flow of a fluid back toward an entry port.

40. A cartridge adapted for use with an analyzer for assaying an enzyme in a fluid sample comprising:

a housing having a sample entry port, overflow chamber, holding chamber, and analysis location,

an airtight entry port closure,

a pump actuated by the analyzer for moving the sample within the cartridge,

one or more reagent deposits in the analysis location comprising at least one substrate capable of reaction with an enzyme in the fluid sample, the reaction of the enzyme forming a detectable reaction product,

a first sensor for detecting the location of the fluid sample, and

a second sensor for detecting the detectable reaction product.

41. The cartridge of claim 40, further including a hydrophobic area comprising a portion of the analysis location.

42. The cartridge of claim 40 wherein the reaction product is detected by an optical sensor.

43. The cartridge of claim 40 wherein the reaction product is an electrochemical species detected by an electrochemical sensor.

44. The cartridge of claim 40 wherein the enzyme is selected from the group consisting of factor VII, factor VIII, factor IX, factor X, factor XI, factor XII, and thrombin.

45. The cartridge of claim 40 wherein the enzyme is thrombin.

46. The cartridge of claim 40 wherein the reagent includes solubility-enhancing components.

47. The cartridge of claim 40 wherein the volume of the fluid sample delivered to the analysis location is metered.

48. The cartridge of claim 40 wherein the reagent includes an electrochemical species other than the substrate and its reaction product.

49. The cartridge of claim 48 wherein the electrochemical species is detectable at a different electrical potential than the substrate and the product.

50. The cartridge of claim 40 wherein substrate or reagent is deposited at more than one site within the analysis location.

51. The cartridge of claim 40 wherein the fluid sample is oscillated past the first and second sensors while in the analysis location.

52. The cartridge of claim 40 wherein the second sensor measures the concentration of reaction product each time the fluid sample is oscillated past the second sensor.

53. The cartridge of claim 40 wherein the reagent comprises a matrix that promotes rapid dissolution into the fluid sample.

54. The cartridge of claim 40 wherein the reagent comprises one or more components selected from the group consisting of a water-soluble polymer, gelatin, agarose, a polysaccharide, polyethylene glycol, polyglycine, a saccharide, sucrose, an amino acid, glycine, a buffer salt, sodium phosphate, HEPES buffer, and a dye molecule.

55. The cartridge of claim 40 further comprising a reagent that promotes the coagulation of blood or a blood derivative.

56. The cartridge of claim 55 wherein the reagent is selected from the group consisting of celite, kaolin, diatomaceous earth, clay, silicon dioxide, ellagic acid, natural thromboplastin, recombinant thromboplastin, phospholipid, and mixtures thereof.

57. The cartridge of claim 40 wherein the first sensor is a conductimetric sensor and the second sensor is an amperometric sensor.

58. The cartridge of claim 57 wherein the analyzer applies a potential to an amperometric sensor with the generation of an electrochemical signal, said signal being proportional to the concentration of the substrate in the fluid sample.

59. The cartridge of claim 57 wherein the analyzer applies a potential to a amperometric sensor with the generation of an electrochemical signal, said signal being proportional to the concentration of the product in the fluid sample.

60. The cartridge of claim 57 wherein hydrolysis of the substrate by thrombin forms a product which reacts at the amperometric sensor with the generation of a signal distinguishable from a signal generated by the substrate.

61. The cartridge of claim 57 wherein the amperometric sensor is microfabricated.

62. The cartridge of claim 57 wherein the conductimetric sensor is microfabricated.

63. The cartridge of claim 57 wherein said amperometric sensor has an applied potential of approximately +0.4V versus a silver-silver chloride electrode.

64. The cartridge of claim 57 wherein said amperometric sensor has an applied potential of approximately +0.1V versus a silver-silver chloride electrode.

65. The cartridge of claim 57 wherein said conductimetric sensor is proximal to the capillary stop and said amperometric sensor is distal from the capillary stop.

66. The cartridge of claim 40 wherein said first or said sensor is comprised of a metal selected from the group consisting of gold, platinum, silver, and iridium.

67. The cartridge of claim 40 wherein said first or said second sensor is coated with a self-assembled thiol film.

68. The cartridge of claim 40 wherein said first or said second sensor is in the shape of an antenna.

69. The cartridge of claim 40 wherein the reagent includes a substance that promotes coagulation of blood.

70. The cartridge of claim 40 wherein the fluid sample is blood or a blood derivative.

71. The cartridge of claim 70 wherein the blood derivative is selected from the group consisting of blood containing an additive or diluent, plasma, serum and plasma or serum containing an additive or diluent.

72. The cartridge of claim 40 wherein the substrate is selected from the group consisting of a tosyl-glycyl-prolinyl-arginyl-, H-D-phenylalanyl-pipecolyl-, and benzyl-phenylalanyl-valyl-arginyl- moiety attached to a moiety selected from the group consisting of an N-phenyl-p-phenylenediamine, and an N-[p-methoxyphenyl-]-p-phenylenediamine moiety.

73. The cartridge of claim 40 wherein the reaction product is selected from the group consisting of N-phenyl-p-phenylenediamine and N-[p-methoxyphenyl-]-p-phenylenediamine moiety.

75. The cartridge of claim 40 wherein the enzyme is selected from the group consisting of glucose oxidase, lactate oxidase, and other oxidoreductases, dehydrogenase based enzymes, alkaline phosphatase and other phosphatases, and serine proteases.

76. The cartridge of claim 40 wherein a sensor is coated with a mercaptoalkanol reagent selected from the group consisting of mercaptoethanol, mercaptopropanol, mercaptobutanol, and mixtures thereof.

77. The cartridge of claim 40 wherein a reagent deposit is in the fluid path.

78. A method of assaying an enzyme in a sample of blood or blood derivative comprising the steps of:

obtaining a sample of blood or blood derivative,

placing the sample into the entry port of a cartridge of claim 40,

closing the entry port,

activating the pump, thereby forcing a sample from the sample chamber into the analysis chamber,

oscillating the sample back and forth in the analysis chamber, and

determining the concentration of the reaction product using the second sensor.

79. The method of claim 78 wherein the pump oscillates the sample in the analysis chamber with the trailing edge of the sample positioned in the region of a selected sensor in order to dissolve the substrate in that portion of the sample near the trailing edge.

80. The method of claim 78 wherein the oscillation is at a frequency in the range of 0.2 to 10 Hertz for a period in the range of 1 to 100 seconds.

81. The method of claims 78 wherein the oscillation is at a frequency in the range of about 1.5 Hertz for a period of about 20 seconds.

82. The method of claim 78 wherein the oscillation is at a frequency of about 0.3 Hertz and the second sensor generates a signal at each oscillation.

83. The method of claim 78 wherein the oscillation is at a frequency sufficient to prevent settling of erythrocytes on a sensor.

84. The method of claim 78 further comprising the step of:

storing an amperometric first sensor signal after a reagent is dissolved.

85. The method of claim 78 further comprising the step of:

analyzing subsequent amperometric sensor signals to determine the maximum rate of change in sensor signal.

86. The method of claim 85 further comprising the step of:

determining a fixed fraction of the maximum rate of change in the sensor signal.

87. The method of claim 85 further comprising the step of:

determining the coagulation parameter from the first sensor signal and the fixed fraction.

88. A method of assaying an enzyme in a sample of blood or blood derivative, comprising the steps of:

introducing the sample into a cartridge which includes an analysis location,

metering a portion of the sample,

moving the metered sample to the analysis location,

mixing the metered sample with reagent at the analysis location,

allowing the enzyme to react with the reagent,

positioning the reacted sample at a sensor, and

detecting the product of the enzyme reaction using the sensor.

89. A single-use cartridge used in combination with an analyzer for determining a coagulation parameter of a sample of blood or blood derivative, comprising;

a cartridge which includes an entry port for receiving a sample, an entry port closure, a holding chamber in communication at a first end with the entry port, and a capillary stop in communication with the holding chamber at a second end, the capillary stop also in communication with an analysis chamber,

the holding chamber in communication with an overflow chamber for receiving and retaining excess sample,

the overflow chamber in communication with a pneumatic pump actuated by the analyzer,

the analyzer actuating the pneumatic pump to displace sample in the holding chamber through the capillary stop into the analysis chamber to deliver a metered portion of the sample into the analysis chamber,

the analysis chamber containing a substrate for the enzyme thrombin capable of dissolving in the metered sample, an amperometric sensor for detecting the product of the reaction between thrombin and the substrate, and a conductimetric sensor for detecting the position of the sample in the analysis chamber,

the amperometric sensor and the conductimetric sensor connected to the analyzer for providing output signals to the analyzer,

the analyzer capable of using the output signal of the conductimetric sensor to actuate the pneumatic pump to control the position of the sample in the analysis chamber,

the analyzer capable of determining the coagulation parameter from the output signal of the amperometric sensor, and

the cartridge containing a hydrophobic area between the capillary stop and the analysis chamber to prevent sample in the analysis chamber from being drawn back into the holding chamber.